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Express Mail No: EL 501 641 199 US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: Pramod K. Srivastava

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AUG 09 2001

Application: 09/750,972

Group Art Unit: 1645

TECH CENTER 1600/2900

Filed: December 28, 2000

Examiner: To be assigned

For: ALPHA (2) MACROGLOBULIN RECEPTOR
AS A HEAT SHOCK PROTEIN RECEPTOR
AND USES THEREOF

Attorney Docket No.: 8449-134

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Pursuant to 37 C.F.R. § 1.102(d), Applicant hereby petitions to make the above-identified application special on the grounds that it relates to the treatment and prevention of cancer. This Petition is accompanied by: (1) a Verified Statement explaining how the invention contributes to the diagnosis, treatment or prevention of cancer, as required by MPEP § 708.02 (X); and (2) Exhibit A: a copy of the pending claims.

The present application discloses methods for treating and preventing cancer through the use of the alpha (2) macroglobulin receptor ("α2MR") as a heat shock protein ("HSP") receptor. In particular, the above-identified application encompasses methods for treating and preventing cancer through the use of the α2MR, methods of identifying molecules that modulate an HSP-α2MR interaction, methods for modulating the immune response by administering compounds that modulate the interaction of HSPs with an α2MR, methods for identifying fragments of an α2MR capable of interacting with HSPs, methods of

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identifying molecules that interact with an α 2MR, methods for detecting an HSP- α 2MR-related disorder, and methods for increasing the immunopotency of a cancer cell by transforming the cell with an α 2MR nucleic acid.

As shown by the accompanying Verified Statement of Daniel Levey, Ph.D., the methods disclosed and claimed in the application provide a promising strategy for treating a variety of different cancers in humans. In view of this factual showing, Applicant submits that the criteria set forth in MPEP § 708.02 (X) are satisfied, and accordingly requests that the Patent and Trademark Office grant this Petition and make this application special.

Pursuant to 37 C.F.R. § 1.17(h), the fee for this petition is believed to be **\$130.00**. Please charge the required fee to Deposit Account No. 16-1150, in the name of Pennie & Edmonds LLP. A copy of this sheet is enclosed for fee purposes.

Respectfully submitted,

Date: August 6, 2001


Adriane M. Antler 32,605
(Reg. No.)

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Part of #8

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For: ALPHA (2) MACROGLOBULIN RECEPTOR AS Attorney Docket No.: 8449-134
A HEAT SHOCK PROTEIN RECEPTOR AND
USES THEREOF

**VERIFIED STATEMENT IN SUPPORT OF PETITION TO
MAKE SPECIAL PURSUANT TO 37 C.F.R. § 1.102(d)**

Assistant Commissioner for Patents
Washington, D.C. 20231

SIR:

I am the Senior Manager of Scientific Affairs of Antigenics Inc., the exclusive licensee of the above-identified patent application. I make this Verified Statement in support of a Petition To Make Special, pursuant to 37 C.F.R. § 1.102(d).

Heat shock proteins ("HSPs") have been shown to play an important role in the treatment of cancer. For example, experimental vaccines based on HSPs complexed to peptides isolated from tumor cells have been shown to cause the regression of pre-existing, metastatic tumors as well as prolong the survival rates of animals in a large number of animal models (Tamura *et al.*, 1997, Science 278(5335):117-20). Noncovalent complexes of HSPs and peptide, purified from cancer cells, can be used for the treatment and prevention of cancer and have been described in PCT publications WO 96/10411, dated April 11, 1996, and WO 97/10001, dated March 20, 1997 (U.S. Patent No. 5,750,119 issued April 12, 1998, and U.S. Patent No. 5,837,251 issued November 17, 1998, respectively (*see* specification of the above identified application, Serial Number 09/750,972, page 3, lines 1-5).

During the last three years, HSPs have been tested in human clinical trials in seven different types of cancer including melanoma, colorectal, kidney, gastric and pancreatic cancers. The results of these trials have been reported at conferences of the American Society of Clinical Oncology and the American Society for Cancer Research. The results showed that immunization with HSPs complexed with peptides isolated from cancerous cells results in a significant positive clinical response in patients with bulky metastatic disease. These studies also suggest that survival of patients is prolonged after treatment with HSP-peptide complexes. Because HSPs are present in all cells in the body, their utility as cancer vaccines is expected to apply to all cancer types.

Many studies have also focused on the mechanism of induction of the immune response by HSP-peptide complexes. These studies have demonstrated that HSP-peptide complexes are powerful activators of T cells, the cells responsible for eradicating cancer cells throughout the body. The instant patent application discloses the identification of an HSP receptor present on dendritic cells called CD91 (previously known to be a receptor for alpha-2-macroglobulin). The Applicant has shown that the HSPs gp96, hsp90, hsp70, and calreticulin bind directly to CD91 and that α 2M inhibits re-presentation of gp96, hsp90, hsp70, and calreticulin-chaperoned antigenic peptides (*see* specification of the instant application, pages 74-87).

Thus, CD91 acts as a HSP receptor that allows extracellular HSP-peptide complexes into dendritic cells. It has been further demonstrated that once inside the cell, the HSP-chaperoned peptides are processed and then re-presented by MHC class I molecules on the cell surface resulting in the generation of a T-cell immune response against the antigens. The crucial role that CD91 is predicted to play in mediating an immune response to cancer suggests that drugs that modulate its activity will be immediately applicable to treating a number of human diseases, including human cancers. Various claims of the instant application are directed to methods for identifying compounds or molecules that modulate the activity of CD91 and its interaction with HSPs. Such identified compounds or molecules potentially can be used as a basis for drug design or cancer therapy because of their potential ability to help activate an immune response against cancerous cells. Related methods claimed in the application, *e.g.*, for modulating the immune response, and for increasing the immunopotency of a cancer cell, may also contribute to the treatment or prevention of cancer.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

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Signature: Daniel Levey Date: July 27, 2001